PART ONE
THE STRUCTURE OF LEUCENOL

PART TWO
ADDITION AND CONDENSATION REACTIONS OF 2-PYRIDONE

BY

VIRON VERNON JONES

B.S., University of Utah, 1940

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
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PART ONE

THE STRUCTURE OF LEUCENOL

Introduction

Leucenol is a natural product obtained from *Leucaena glauca Bentham,* and from *Mimosa pudica Linn.* Degradation studies indicate that the product is an α-amino acid derived from one of the dihydroxypyridines (1-4).

It was the purpose of the present investigation to further elucidate the structure of leucenol through a series of chemical studies.

Discussion Of Results

N-*n*-Propyl-2-pyridone and 2-*n*-propoxypyridine have been prepared and subjected to the action of boiling hydrobromic acid. The former is unchanged but the latter is hydrolyzed to 2-pyridone. β-(N-2-Pyridone)-propionic acid, a compound analogous to leucenol was prepared. This acid cleaves by pyrolysis to 2-pyridone and acrylic acid; it is cleaved by strong alkali to 2-pyridone; it is unaffected by boiling hydrobromic acid. These data together with that already known for leucenol (3) support the hypothesis that the side chain in leucenol is attached to the nitrogen atom of the pyridine rather than to the oxygen atom. The side chain attached to a carbon atom of the pyridine is unlikely in view of the mild conditions which bring about cleavage.

Leucenol pyrolyzate was obtained in the form of colorless needles which crystallize as an unstable hydrate from water. Upon treatment with diazomethane N-methyl-3-methoxy-4-pyridone was obtained. The pyrolyzate was found to be identical to 3-hydroxy-4-pyridone. The structure of leucenol is therefore proposed to be α-amino-β-(N-3-hydroxy-4-pyridone)-propionic acid.

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PART TWO

ADDITION AND CONDENSATION REACTIONS OF 2-PYRIDONE

Introduction

The purpose of this investigation was to study the addition and condensation reactions of 2-pyridone which might lead to the preparation of a 2-pyridone analog of leucenol. 2-Pyridone was used in the place of 4-pyridone or 3-hydroxy-4-pyridone because of greater accessibility. These reactions were to be used as models for the synthesis of leucenol.

Discussion Of Results

Products were isolated and described for the reaction of 2-pyridone with the following reagents: Chloroacetaldehyde, bromopyruvic acid, butadienesulfone, α-acetamidoacrylic acid, chloroacetic acid, α,β-dibromopropionic acid, α-bromoacrylic acid, and ethyl α-bromo-β-ethoxypropionate. Treatment of β-(N-2-pyridone)-propionic acid with bromine and red phosphorus yielded β-(N-3,5-dibromo-2-pyridone)-propionic acid. The 2-pyridone analog of leucenol was prepared from the hydrolysis of the product obtained from 2-pyridone and α-acetamidoacrylic acid. A similar reaction was utilized by Adams and Johnson for the synthesis of leucenol (1).

The product obtained from the reaction of 2-pyridone and α-bromoacrylic acid was treated with ammonia to yield a compound which was not an α-amino acid, but was shown to be α-(N-2-pyridone)-β-aminopropionic acid. Upon treatment with alkali both the 2-pyridone bromoacrylic acid adduct and its product with ammonia yielded α-(N-2-pyridone)-β-hydroxypropionic acid which was also synthesized from glycidic acid and 2-pyridone. An ethyleneimmonium bromide structure has been proposed for the 2-pyridone α-bromoacrylic acid adduct by analogy to products obtained by Cromwell (2) from the reaction of secondary amines with α-bromo-α,β-unsaturated ketones.

The 2-pyridone α-bromoacrylic acid adduct yielded a betaine type of compound upon treatment with one mole of silver oxide. Treatment with one-half mole of silver oxide resulted in a betaine hemihydrobromide. A double salt-like structure was proposed for this product.

The 2-pyridone α-bromoacrylic acid adduct was hydrogenated with palladium on charcoal to yield a syrup which upon treatment with ammonia yielded α-(N-2-piperidone)-β-aminopropionic acid. When platinum oxide was used as the catalyst, a product was obtained which proved to be the hydrobromide of α-hydroxy-β-piperidinopropionic acid. This latter compound was synthesized from piperidinoacetaldehyde through the cyanohydrin, and also from piperidine and β-chlorolactic acid. A mechanism was proposed to explain the product obtained by the hydrogenation of the 2-pyridone α-bromoacrylic acid adduct with platinum oxide.

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VITA

The author was born June 9, 1917 at Cedar City, Utah. He attended various schools in Utah and California, graduating from high school in 1936. The years 1936 to 1938 were spent at the Dixie Junior College. He entered the University of Utah in 1938 receiving the degree of Bachelor of Science in 1940. One year of graduate work was done at the same institution after which a position was taken with the United States Bureau of Mines. He served with the United States Armed Forces from February 1942 to January 1946. The Graduate School, University of Illinois was attended from March 1946 to June 1949. A Cincinnati Chemical Works Fellowship was held during the period 1946-1949.

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